EDITORIAL COMMENT†

VIRUS AGGLUTINATION

Successful applications of the new technique of specific agglutination of virus-coated bacteria are currently reported by Roberts and Jones [1] of the Department of Bacteriology, St. Louis University. Data thus far published by the St. Louis investigators suggest that the new technique may be of wide clinical application and may necessitate numerous revisions of basic concepts in many fields of practical diagnosis and therapy.

About fifteen years ago it was shown by Freund,[2] and has been subsequently confirmed by other investigators,[3] that if a soluble protein is adsorbed on the surfaces of small particles, the coated particles are readily agglutinated with the antiserums of animals immunized against this protein. Collodion particles were used by the earlier investigators. Jones,[3] however, found that certain nonpathogenic bacteria are more readily coated by alien proteins, heat-killed B. prodigiosus, for example, being successfully coated with horse or beef proteins by mere incubation in the presence of horse or beef serum. After thorough washing with saline solution, the exposed bacterial cells can be agglutinated by minute traces of homologous rabbit precipitins.

Quantitative comparisons showed that the agglutination test is at least one hundred times more delicate than the routine precipitin test with the same protein. In a rabbit injected with a single subcutaneous dose of 0.1 cubic centimeter of horse serum per kilogram of body weight, for example, the routine precipitin test shows no trace of specific antibody formation till the fourth day. Using a suspension of horse-protein coated B. prodigiosus as the diagnostic agent, however, specific antibody formation may be demonstrable as early as twenty-four hours, the titer rising to a maximum by the fourth day. After this, there is a precipitous fall in titer, antibodies, however, being demonstrable for many weeks after their apparent complete disappearance as shown by the conventional precipitin reaction. Applying this new diagnostic reagent to human beings who had received antigenic foreign proteins, Roberts and Jones found that in man also antibodies can be detected much earlier than currently assumed and that they present in significant amounts much longer than now believed.

Since the new agglutination technique is capable of detecting antibodies in quantities too small to be revealed by routine methods, there is a suggested necessity of an experimental restudy of many fields of clinical immunology. Applying the new technique to a study of St. Louis type encephalitis, for example, Roberts and Jones found B. prodigiosus could be effectively coated with the virus by incubating the heat-killed microörganisms in a saline emulsion of infected mouse brain. That the virus was actually adsorbed on the bacteria was indicated by the observation that after repeated washings with saline solution, such coated cells will reproduce typical encephalitis upon intranasal implantation in mice.

Suspensions of encephalitis-coated bacteria were used as diagnostic antigens. Rabbits repeatedly injected with encephalitis brain suspensions yielded antisera which agglutinated the virus-coated bacteria in dilutions as high as 1:512, control tests with the serum of normal rabbits and of rabbits immunized against normal mouse brain, giving negative results. In convalescent human beings the same specific agglutination reaction occurred in dilutions as high as 1:128. Eighty per cent of all supposedly normal individuals gave positive reaction usually in dilutions higher than 1:8. In most, but not all, instances the agglutinin titer is correlated with the viricidal index. Experiments are now under way to apply the same technique to poliomyelitis and to other conditions in which low titer antibodies conceivably play an important clinical rôle. Applications to allergy, to the toxemia of pregnancy, and to malignant diseases will be awaited with interest.

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MENSTRUAL TOXIN

Demonstration of a highly toxic euglobulin in menstrual discharge is an interesting confirmation of a popular medical belief.

In order to study the physiological properties of the menstrual flow, Smith and Smith,[1] of the Fearing Research Laboratory, Brookline, Massachusetts, collected, by means of soft rubber cups, thirty-seven specimens of menstrual discharge from normal parous women. Pooled samples from each woman were placed in the refrigerator, control samples of citrated venous blood being collected from the same individuals.

The Brookline gynecologists found that menstrual discharge is lethally toxic for normal, mature female rats, if injected subcutaneously in 0.1 to 1.0 cubic centimeter doses. Toxicity was greatest during the preëstrus period. Within 24 hours after the first injection, the animals were usually "hunched up," water intake was increased, the nose and inner canthi of the eyes were encrusted with blood, and a firm, wide area of edema had developed about the site of the injection. Death usually resulted within 48 hours. At autopsy widespread edema, with capillary hemorrhages, were noted in the lungs

† This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comments by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California Medical Association to submit brief editorial discussions suitable for publication in this department. No presentation should be over five hundred words in length.

1 Roberts, E. C., and Jones, L. R.: Proc. Soc. Exper. Biol. and Med., 47:11, 74 (May), 1941.

2 Freund, Jules: Amer. Rev. The., 12:124, 1925.

3 Mudd, S.: et al.: Jour. Exper. Med., 52:313, 1930. Jones, F. S.: Jour. Exper. Med., 46:303, 1927; 48:183, 1928. Delues, Edna: Jour. Infect. Dis., 60:55, 1937.

1 Smith, O. W., and Smith, G. V. S.: Proc. Soc. Exp. Biol. and Med., 44:100 (May), 1940.

and other internal organs, with occasional blood in the urinary bladder. The most constant lesion was in the adrenal cortex. In rats that died early, adrenal hemorrhages might be the only demonstrable lesion. With later deaths, widespread adrenal necrosis was microscopically demonstrable.

If the injections were started at the beginning of the post-estrus period, the animals were more likely to survive, and to develop a relative immunity. Male rats and spayed females are highly refractory. A simultaneous injection of estrogen increases the toxicity in rats with intact ovaries; but it has no adjuvant toxic action in spayed female rats. From this the Brookline investigators conclude that "susceptibility to the menstrual toxin depends upon the presence of the ovaries," a conclusion confirmed by simultaneous injection of ovarian emulsions into spayed females which renders them susceptible. Large amounts of progesterone completely protect female rats from this toxin. From this, too, the Smiths conclude that the corpus luteum functions as an antitoxic endocrine. Chemical analyses show that the toxin is nondialysable, and found in greatest concentration in the euglobulin fraction of the menstrual discharge.

Mature female rabbits are extremely susceptible to this toxin, a single subcutaneous injection of 1 cubic centimeter often resulting in death within 48 hours. Repeated sublethal doses will immunize rabbits against the euglobulin, the resulting antiserum protecting female rats against multilethal doses of menstrual discharge.

Bacteriological examinations and control tests, with purposefully contaminated venous blood, rule out the probability that the menstrual toxin is a product of bacterial action. The toxin is apparently a specific endometrial product, which possibly functions as a hitherto unrecognized hormonal regulator of the normal sexual cycle.

The fact that the menstrual toxin is antigenic, and that its maximum toxic effects are manifest only under certain hormonal conditions, render the alleged toxic menstrual euglobulin a very promising instrument of immuno-endocrinologic research. A considerable amount of Smith's alleged effects, however, cannot be explained by our present knowledge of endocrinology and, therefore, should not be accepted without confirmation.

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Of the various causes of accidental death, in the United States, motor vehicles lead; indeed, in 1939 they were responsible for 35 per cent of all such deaths, killing a total of 32,600 persons; in fact, a person died every 16 minutes throughout the year from automobile accidents. The number of deaths was two and one-half times those caused by syphilis, equal to those caused by diabetes, and one-half of those caused by tuberculosis. More children were killed by traffic accidents in 1939 than died from diptheria, measles, scarlet fever, and whooping cough combined. Besides the fatalities, 1,150,000 other persons were injured. Of every five who died in traffic accidents, two were pedestrians.

ORIGINAL ARTICLES

ADMINISTRATIVE PSYCHIATRY*

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IT is my purpose today to present a brief discussion of administrative psychiatry, not in general terms, but in the more concrete terms of policies and operations of the State Department of Institutions, which are now in effect or expected to be put in effect in the near future.

In the field of psychiatry, science has outrun its applications; and I have conceived the main task of the Department to be that of introducing, in our practice, all measures and procedures that would be justified by the knowledge in our field which is well established but pigeonholed in scientific archives.

Some of these measures and procedures are new for California; but most of them had already been introduced, to some extent, during previous administrations, and we have been seeking merely to encourage their more systematic and more complete development.

OVERCROWDING IN MENTAL HOSPITALS

The mental hospitals of our State, like those of all other states in the Union, have been for many decades, and still are, in a condition of overcrowding to an extent averaging between 15 and 30 per cent beyond their capacity. During the past ten years we have been spending an average of $3,200,000 per biennium for major construction; but, at the same time, the net increase of the population of our mental hospitals has been at the rate of 840 patients per year, and for this reason the construction of new hospitals, or of additions to existing hospitals, has had no appreciable effect on the overcrowding.

The principal measures that we have planned for coping with this problem are: first, provision of facilities for prevention, early diagnosis, and timely treatment of mental disorders, with a view to stemming the flood of commitments of patients in advanced and, therefore, more chronic stages of their illness, who become, for the most part, permanent inmates of our institutions; and, second, extension of our parole system and other devices for extramural care of chronic, but inoffensive mental patients.

In other words, measures for the relief of overcrowding now consist not only of construction of additions to our institutions, but also of diminishing our intake of patients and increasing their outgo.

THE LANGLEY PORTER CLINIC

Appropriations have been obtained from the Legislature for the establishment of an acute neuropsychiatric unit on the campus of the Medical

* From the office of the director of the Department of Institutions, State of California.
Read before the Second General Meeting at the seventieth annual session of the California Medical Association, Del Monte, May 5–8, 1941.